

**Amendments to the Claims**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims**

Claim 1. (Currently Amended): A method for determining the type of biocompatible polymer, the extent of modification, and the conditions for modification of ~~modifying~~ a therapeutic agent with a biocompatible polymer; to prevent host-mediated inactivation of said therapeutic agent when covalently modified by said biocompatible polymer, comprising:

(a) ~~(1)~~ assaying the biological activity of a first modified therapeutic agent after said first modified therapeutic agent has been administered to a subject, wherein said first modified therapeutic agent is covalently modified with a biocompatible polymer;

(b) ~~(2)~~ assaying the biological activity of said first modified therapeutic agent after at least one booster dose of said first modified therapeutic agent has been administered to said subject;

(c) ~~(3)~~ assaying the biological activity of a second modified therapeutic agent after said second modified therapeutic agent has been administered to a subject ~~carrying out (1) and (2) with a second modified therapeutic agent~~, wherein said second modified therapeutic agent is covalently modified with a biocompatible polymer and wherein at least one condition selected from the group consisting of the type of biocompatible polymer, the extent of modification, and the conditions for modification differs from the conditions of ~~is modified differently from~~ said first modified therapeutic agent;

(d) assaying the biological activity of said second modified therapeutic agent after at least one booster dose of said second modified therapeutic agent has been administered to said subject; and

(e) ~~(4)~~ comparing the biological activity of said first modified therapeutic agent with the biological activity of said second modified therapeutic agent to select the type of biocompatible polymer, the extent of modification, and the conditions for modification that

prevent host-mediated inactivation of said therapeutic agent when covalently modified by said biocompatible polymer.

Claim 2. (Previously Presented): The method of claim 1, wherein said second modified therapeutic agent is modified with the same biocompatible polymer as said first modified therapeutic agent.

Claim 3. (Previously Presented): The method of claim 2, wherein said biocompatible polymer is polyethylene glycol (PEG).

Claim 4. (Original): The method of claim 3, wherein said PEG is selected from the group consisting of mono-methoxy succinimidyl butanoate (SBA)-PEG, succinimidyl carbonate (SC)-PEG, aldehyde (ALD)-PEG, and succinimidyl propionate (SPA)-PEG.

Claim 5. (Previously Presented): The method of claim 1, wherein said second modified therapeutic agent is modified to the same extent as said first modified therapeutic agent.

Claim 6. (Previously Presented): The method of claim 1, wherein said second modified therapeutic agent and said first modified therapeutic agent are modified with different biocompatible polymers.

Claim 7. (Currently Amended): The method of claim 1, wherein said therapeutic agent comprises is a polypeptide.

Claim 8. (Original): The method of claim 7, wherein said polypeptide is used to treat viral infections in patients in need of treatment thereof.

Claim 9. (Original): The method of claim 7, wherein said polypeptide is used to treat cancer in patients in need of treatment thereof.

Claim 10. (Original): The method of claim 7, wherein said polypeptide has a monomeric molecular weight of about 300 daltons to about 300,000 daltons.

Claim 11. (Original): The method of claim 7, wherein said polypeptide is used to lower glutamine levels in a subject.

Claim 12. (Original): The method of claim 7, wherein said polypeptide is used to lower asparagine levels in a subject.

Claim 13. (Original): The method of claim 7, wherein said polypeptide is used to lower asparagine and glutamine levels in a subject.

Claim 14. (Withdrawn): The method of claim 1, wherein said therapeutic agent is a nucleic acid.

Claim 15. (Withdrawn): The method of claim 14, wherein said nucleic acid is used to treat a viral infection in patients in need of treatment thereof.

Claim 16. (Withdrawn): The method of claim 14, wherein said nucleic acid is used to treat cancer in patients in need of treatment thereof.

Claim 17. (Currently Amended): A method of preparing a pharmaceutical composition where host-mediated inactivation is prevented, comprising selecting the type of biocompatible polymer, the extent of modification, and the conditions for modification ~~ascertaining the modification conditions~~ of a therapeutic agent by the method of claim 1 and modifying said therapeutic agent according to the type of biocompatible polymer, the extent of modification, and the conditions for modification selected ~~said modification conditions~~.

Claim 18. (Original): The method of claim 17, wherein said pharmaceutical composition further comprises an excipient.

Claim 19. (Original): The method of claim 18, wherein said excipient protects said therapeutic agent during lyophilization.

Claim 20. (Original): The method of claim 17, wherein said therapeutic agent comprises glutaminase-asparaginase.

Claim 21. (Currently Amended): The method of claim 20, wherein said therapeutic agent comprises *Pseudomonas* glutaminase-asparaginase.

Claim 22. (Original): The method of claim 21, wherein said *Pseudomonas* glutaminase-asparaginase is modified with polyethylene glycol.

Claim 23. (Withdrawn): The pharmaceutical composition prepared by the method of claim 17, wherein said pharmaceutical composition comprises a glutaminase-asparaginase that has been modified with succinimidyl carbonate polyethylene glycol 5000 (SC-PEG 5000), wherein said glutaminase-asparaginase is modified to an extent of from about 21% to about 49% by SC-PEG 5000, and wherein said composition prevents host-mediated inactivation.

Claim 24. (Withdrawn): The composition of claim 23, wherein said glutaminase-asparaginase is modified from about 26% to about 36% by SC-PEG 5000.

Claim 25. (Withdrawn): The composition of claim 24, wherein said glutaminase-asparaginase is modified about 31% by SC-PEG 5000.

Claim 26. (Withdrawn): The pharmaceutical composition prepared by the method of claim 17, wherein said pharmaceutical composition comprises a glutaminase-asparaginase that has been modified with mono-methoxy succinimidyl butanoate polyethylene glycol 5000 (SBA-PEG 5000), wherein said glutaminase-asparaginase is modified from about 25% to about 58% by SBA-PEG 5000, and wherein said composition prevents host-mediated inactivation.

Claim 27. (Withdrawn): The composition of claim 26, wherein said glutaminase-asparaginase is modified from about 30% to about 40% by SBA-PEG 5000.

Claim 28. (Withdrawn): The composition of claim 27, wherein said glutaminase-asparaginase is modified about 35% by SBA-PEG 5000.

Claim 29. (Withdrawn): The pharmaceutical composition prepared by the method of claim 17, wherein said pharmaceutical composition comprises a glutaminase-asparaginase that has been modified with aldehyde polyethylene glycol 2000 (ALD-PEG 2000), wherein said glutaminase-asparaginase is modified from about 45% to about 65% by ALD-PEG 2000, and wherein said composition prevents host-mediated inactivation.

Claim 30. (Withdrawn): The pharmaceutical composition prepared by the method of claim 17, wherein said pharmaceutical composition comprises a glutaminase-asparaginase that has been modified with succinimidyl propionate polyethylene glycol 5000 (SPA-PEG 5000), wherein said modified glutaminase-asparaginase is modified from about 25% to about 65% by SPA-PEG 5000, and wherein said composition prevents host-mediated inactivation.

Claim 31. (Withdrawn): The composition of claim 30, wherein said glutaminase-asparaginase is modified from about 40% to about 55% by SPA-PEG 5000.

Claim 32. (Withdrawn): A composition comprising a glutaminase-asparaginase, wherein said glutaminase-asparaginase has been modified with succinimidyl carbonate polyethylene glycol 5000 (SC-PEG 5000) to an extent of about between 21% and 49%.

Claim 33. (Withdrawn): The modified therapeutic composition of claim 32, wherein said glutaminase-asparaginase has been modified to an extent of about between 26% and 36%.

Claim 34. (Withdrawn): The modified therapeutic composition of claim 33, wherein said glutaminase-asparaginase has been modified to an extent of about 31%.

Claim 35. (Withdrawn): A composition comprising a glutaminase-asparaginase, wherein said glutaminase-asparaginase has been modified with succinimidyl butanoate polyethylene glycol 5000 (SBA-PEG 5000) to an extent of about between 25% and 58%.

Claim 36. (Withdrawn): The modified therapeutic composition of claim 35, wherein said glutaminase-asparaginase has been modified to an extent of about 30% to 40%.

Claim 37. (Withdrawn): The modified therapeutic composition of claim 36, wherein said glutaminase-asparaginase has been modified to an extent of about 35%.

Claim 38. (Withdrawn): A composition comprising a glutaminase-asparaginase, wherein said glutaminase-asparaginase has been modified with aldehyde polyethylene glycol 2000 (ALD-PEG 2000) to an extent of about between 45% and 65%.

Claim 39. (Withdrawn): A composition comprising a glutaminase-asparaginase, wherein said glutaminase-asparaginase has been modified with succinimidyl propionate polyethylene glycol 5000 (SPA-PEG 5000) to an extent of about between 25% and 65%.

Claim 40. (Withdrawn): The modified therapeutic composition of claim 39, wherein said glutaminase-asparaginase has been modified to an extent of about 40% to 55%.

Claim 41. (New): The method of claim 1, wherein the subject administered the first modified therapeutic agent is different from the subject administered the second modified therapeutic agent.